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EVALUATION OF WRAIR MICROANALYZER FOR BODY FLUIDS.(U)
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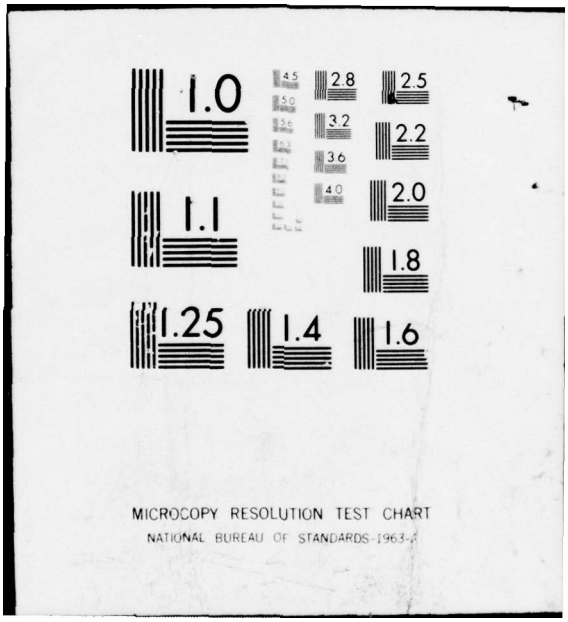
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REPORT 7615

EVALUATION OF WRAIR MICROANALYZER FOR BODY FLUIDS

FINAL REPORT

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The WRAIR Microanalyzer for body fluids was evaluated at five medical treatment facilities. The instruments were operated by a laboratory technician and/or laboratory officer. Glucose content was analyzed by an enzymatic method. Overall, the five units produced very precise results at a fast rate with minimal reagent and sample consumption.

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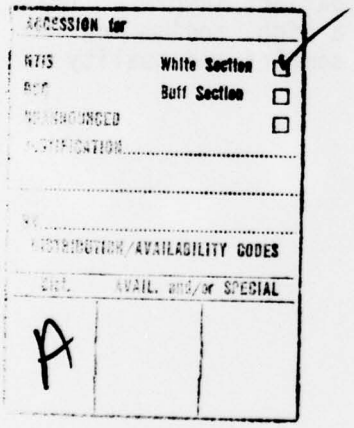
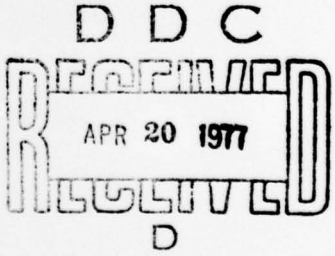
PREFACE

On 29 October 1974, the U.S. Army Medical Research and Development Command (USAMRDC), Washington, DC, tasked the U.S. Army Medical Bioengineering Research and Development Laboratory (USAMBRDL), Fort Detrick, MD with the redesign and evaluation of the "WRAIR Microanalyzer for Body Fluids." Under Work Unit 3A062110A816.00.017, redesign was accomplished and ten prototypes fabricated. Five of those prototypes were evaluated in medical treatment facilities (both military and non-military). This report presents the results of that evaluation and constitutes the final report of the work unit.





INTRODUCTION

Five systems were evaluated for a period of approximately two months at the following local government installations - Fort Belvoir, Rader Clinic, Aberdeen Proving Ground, University Hospitals (Baltimore, MD) and Veterans' Administration Hospital (Baltimore, MD). The instruments were operated by either a laboratory technician and/or a laboratory officer. Glucose content was analyzed by an enzymatic method (Trinder). The developmental test plan should be consulted for details.

EVALUATION PROTOCOL

The plan is divided into two main sections. These sections will henceforth be referred to as the baseline section and the precision section. The baseline period is ten (10) running days long, separated into twofive-day "weeks" with a two-day break between them to simulate weekend shutdown. On each day of this baseline period, two runs are performed, one in the morning and one in the afternoon. Each run consists of randomly chosen hospital patient specimens, with nine (9) quality control samples interspersed with the patient samples. The quality control samples include three each of a high, medium and low concentration material. The order of patient samples and quality control materials is illustrated in Table I.

TABLE 1

BASELINE SECTION WORKSHEET

RUN TWICE A DAY

Test Glucose

Date (MO-DAY) _____
Day (1-10) _____
Run (AM or PM) _____

Sample Position		Sample Position	
35.	50 mg Std	18.	Mid QC _____
36.	50 mg Std	19.	100 mg Std
37.	100 mg Std	20.	100 mg Std
38.	200 mg Std	21.	Sample
39.	300 mg Std	22.	Sample
40.	H_2O	23.	Lo QC _____
1.	Sample	24.	Sample
2.	Sample	25.	Sample
3.	Hi QC _____	26.	Hi QC _____
4.	Sample	27.	Sample
5.	Sample	28.	Lo QC _____
6.	Mid QC _____	29.	100 mg Std
7.	Sample	30.	100 mg Std
8.	Lo QC _____		
9.	100 mg Std		
10.	100 mg Std		
11.	Sample		
12.	Sample		
13.	Mid QC _____		
14.	Sample		
15.	Sample		
16.	Hi QC _____		
17.	Sample		

Standard Curve

Slope _____

Y-intercept _____

Correlation Coefficient _____

The precision section is performed after the completion of this initial baseline period. The precision protocol requires fifteen running days, broken into three simulated five-day "weeks". On each running day of the precision section two runs (morning and afternoon) are required with each run consisting of twenty-four samples (six quality control (QC) samples and six sets of three samples each) as described below. A specific run sequence layout is provided in Table 2 which also serves as the form for data recording. A separate sheet is provided for each run. Precision is evaluated over the entire period, rather than on a daily basis.

Three levels of material are employed for all quality control samples used during the protocol. The "high" material contains a concentration of the component being analyzed at a level considerably above the normal range and approaching the upper limit of the linear range of the test system. The "mid" level material contains a concentration near the midpoint of the normal range. The "low" material is near the lower limit of the linear range of the test system. Stable frozen human plasma pools are used.

TABLE 2

PRECISION WECTION WORKSHEET

Test Glucose

Date (MO-DAY) _____
Day (1-15) _____
Run (AM or PM) _____

Sample Position		Sample Position	
35.	50 mg Std	17.	
36.	50 mg Std	18.	Lo QC _____
37.	100 mg Std	19.	100 mg Std
38.	200 mg Std	20.	100 mg Std
39.	300 mg Std	21.	
40.	H_2O	22.	
1.		23.	
2.		24.	Hi QC _____
3.		25.	
4.	Mid QC _____	26.	
5.		27.	
6.		28.	Mid QC _____
7.		29.	100 mg Std
8.	Lo QC _____	30.	100 mg Std
9.	100 mg Std		
10.	100 mg Std		
11.		Standard Curve	
12.		Slope _____	
13.		Y-intercept _____	
14.	Hi QC _____	Correlation Coefficient _____	
15.			
16.			

RESULTS

In every analytical run a standard curve was made and followed by repeated analysis of two 100 mg/dl standards at regular intervals. All results were calculated by manual entry of each peak height into a Hewlett Packard 9810A programmable calculator. A least squares fit was applied to the standard curve with the regression parameters listed. The slope was used to calculate all results within a single analytical run. Each sample was calculated using a y-intercept value that was determined by its relative position between two sets of standards. In this way any systematic drift that occurred was cancelled out in the calculations. A finite amount of drift always exists in continuous flow analyzers due to small but constantly changing flow rates.

Table 3 summarizes the statistical results for the Baseline Section and Table 4 for the Precision Section. As expected, the coefficient of variation was found to increase as the quantity of glucose measured decreases. For the first one and one-half days of baseline run at University Hospital there was a consistent abnormal elevation in values for the Hi QC. The reason for this remains unexplained. This accounts for their higher mean and coefficient of variation. At Fort Belvoir, there was a single day (#9) during the baseline section where the results for the Hi QC were abnormally low. This may have been due to deterioration of the specimen, since for both instances the Mid QC and Lo QC were within their expected ranges. It does not appear to be an instrument problem. When taking into account that the coefficient of variation represents variation in the same frozen samples over a five week period, the values obtained are exceptionally good.

The coefficients of variation found during the baseline section were slightly higher for the VA hospital than at other locations. This was due to numerous instances of bubble entrapment in their flow cell which produced marked baseline shifts. Rader Clinic also had similar difficulties. Most of the error due to significant baseline shifts was corrected in our method of calculating the results. An excellent example of this is illustrated in Table 5. This data is taken from the VA hospital on run 7 A.M. for the baseline section. If no correction is made for baseline shift the errors are highly significant as may be observed in the uncorrected column. The corrected values very closely approach the actual values.

TABLE 3

SUMMARY OF RESULTS FOR BASELINE SECTION

Glucose mg/dl

		Lo QC	Mid QC	Hi QC
Fort Belvoir	$\bar{X}$ *	51	94	247
	n	2.6	2.6	9.1
	C.V.	5.2%	2.8%	3.7%
Rader Clinic	$\bar{X}$ *	49	95	247
	n	2.9	3.5	4.6
	C.V.	5.8%	3.7%	1.9%
Aberdeen PG	$\bar{X}$ *	49	96	252
	n	1.7	2.6	5.2
	C.V.	3.4%	2.7%	2.0%
Univ Hosp (Balto)	$\bar{X}$ *	51	99	254
	n	2.4	3.2	10
	C.V.	4.7%	3.2%	4.1%
Vets Hosp (Balto)	$\bar{X}$ *	48	95	252
	n	3.2	3.0	10
	C.V.	6.7%	3.2%	4.1%

*Average of 10 days, two runs per day and 3 values per run

TABLE 4

SUMMARY OF RESULTS FOR PRECISION SECTION

Glucose mg/dl

		Lo QC	Mid QC	Hi QC
Fort Belvoir	$\bar{X}$ *	53	94	246
	n	3.3	2.3	5.1
	C.V.	6.2%	2.4%	2.1%
Rader Clinic	$\bar{X}$ *	51	94	243
	n	2.9	2.3	4.0
	C.V.	5.7%	2.4%	1.7%
Aberdeen PG	$\bar{X}$ *	50	95	252
	n	2.0	2.7	4.8
	C.V.	4.0%	2.9%	1.9%
Univ Hosp (Balto)	$\bar{X}$ *	50	95	246
	n	2.5	2.1	3.7
	C.V.	4.9%	2.2%	1.5%
Vets Hosp (Balto)	$\bar{X}$ *	50	96	254
	n	3.0	2.4	3.6
	C.V.	5.9%	2.5%	1.4%

*Averaged over 15 days, 2 runs per day, 6 duplicates per run

TABLE 5

CALCULATOR CORRECTION FOR BASELINE DRIFT

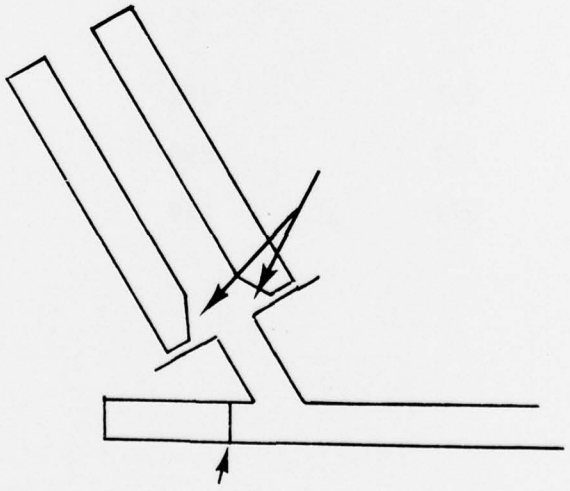
VA Hospital Day 7 A.M. - A significant baseline shift occurred between the beginning and end of run.

	UNCORRECTED	CORRECTED	ACTUAL VALUE
Lo QC	59	47	
	72	46	48
	79	47	
Mid QC	107	98	
	114	97	95
	117	95	
Hi QC	257	252	
	269	250	252
	279	249	

PROBLEMS

The most important information to be gained from this evaluation is recognition of problems that occur and discovery of their causes. This type of information is useful in the design and construction of newer units.

There were numerous problems that occurred during the evaluation period. The main problem resulted from the modified design of the optical flow-cell. The flow-cell produced for this series of instruments was changed significantly from the original design in an attempt to make a better flow-cell. Unfortunately, these changes produced effects opposite to those desired. As it turned out only one out of nine flow-cells produced worked well enough to be used in the evaluation. Proper operation of the system is critically dependent on passage of the bubbled stream through the flow-cell without disruption. The majority of flow-cells resulted in a breakup of the bubble pattern and would then entrap fragments of these bubbles in the optical path. There were two reasons for this problem. Upon dismanteling the flow-cells it was observed that the cylindrical stems that enter the flow-cell block were reamed out so as to prevent a smooth interface betwen the block and stem (See Figure I).



Schematic drawing of flow cell indicating areas trapping bubbles and disrupting flow patterns.

The area that has been reamed out (shown by arrows) traps bubbles and causes fragmentation. Another problem is that the quartz rods were not positioned far enough into the flow-cell as thoroughly discussed in an article by Neeley, et al (1). By not extending slightly into the entering and exiting stream an excellent bubble trap was created. Furthermore, an additional problem was created by allowing the outside ends of the quartz rods to protrude outside the flow-cell block. In this position, the quartz base is easily chipped. In the original design the faces were slightly countersunk. Several flow-cells leaked solution around the quartz rods into the detector lens assemblies due to improper fit.

It is important to note that at this point in time the perfect optical flow-cell has not yet been designed and constructed. All designs explored will occasionally entrap bubbles. The originally designed flow-cell turns out to have the fewest problems but the search should continue for a more trouble free flow-cell design.

The second major problem that occurred in four out of five units was excessive intermittent noise that was due to the numerous ground loops found in the wiring configuration of the main processor box. Whenever dealing with high impedance signals all ground loops must be identified and avoided. The solution was to rewire the grounding systems using heavy wire. All commons should be tied at a single point.

Minor problems included fluid leaks in the fittings and dialyzers. Virtually all of the dialyzers and some of the fittings leaked fluid around the points where the nipples were inserted into the blocks. In all cases the nipples were only secured by treatment with chloroform solvent. The solution to this problem was to secure all nipples in place with epoxy glue. Because of the short distance that the nipples were inserted into the dialyzer blocks they were unusually fragile and easily pulled out of the block. It is recommended that they be inserted to a greater depth.

A potential source of electronic noise to be avoided was the inclusion of both +5 volt direct current power to the lamp and the 110 volt alternating current to the colorimeter from within the same shielded cable. Proper operation of the entire system depends on using "clean" direct current signals and the 110 volt alternating current should always be kept as far away from these direct current signals as possible. The interference filter chosen turned out to have a life of less than two years. A better quality filter set should be used.

CONCLUSION

Overall, the five units produced very precise results at a fast rate (120 samples/hr) with minimal reagent (less than ul/sample) and sample consumption (less than 250 ul/sample). The problems that occurred were readily identified and their solutions may be incorporated into future units.

REFERENCES

Neeley, W.E., Wardlaw, S.C., Yates, T., Hollingsworth, W.C. and Swinnen, M.E.T., Clin Chem 22, 227 (1976)